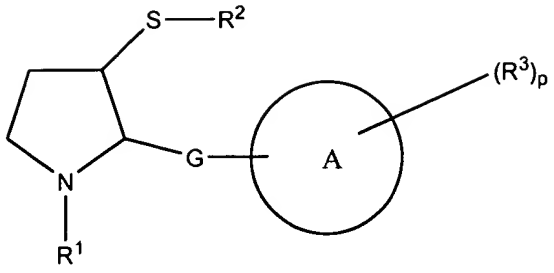


wherein:

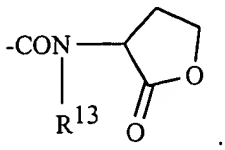
R^1 is selected from H; -C_{1-4}alkyl; -CO-C_{1-4}alkyl; -CO-O-C_{1-4}alkyl; -CO-O-C_{2-4}alkenyl; -C_{1-4}alkylene-CONR^{4}R^5 (wherein R^4 and R^5 are independently selected from H and C_{1-4}alkyl); -C_{1-4}alkylene-COOR^6 (wherein R^6 is selected from H and C_{1-4}alkyl); -C_{1-3}alkylene-Ph and -CO-O(CH $_2$)$_n$Ph wherein the phenyl groups in -C_{1-3}alkylene-Ph and -CO-O(CH$_2$)$_n$Ph are optionally substituted by R^a and/or R^b and R^a and R^b are independently selected from C_{1-4}alkyl, halogen, hydroxy, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, amino, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, C_{1-4}alkanoylamino, nitro, cyano, carboxy, carbamoyl, C_{1-4}alkoxycarbonyl, thiol, C_{1-4}alkylsulfanyl, C_{1-4}alkylsulfinyl,C_{1-4}alkylsulfonyl and sulfonamido; and n=0-4;

R^2 is selected from H; -C_{1-4}alkyl; -COC$_{1-4}$alkyl; and -COOC$_{1-4}$alkyl; and -C_{1-3}alkylene-Ph optionally substituted on the phenyl ring by R^a and/or R^b;

R^3 is selected from H; OH; CN; CF_3; NO_2; -C_{1-4} alkyl; -C_{1-4}alkylene-R^7; -C_{2-4}alkenylene-R^7; -C_{2-4}alkynylene-R^7; R^7; OR^7 (where R^7 is selected from phenyl, naphthyl, a 5-10 membered monocyclic or bicyclic heteroaryl ring containing up to 5 heteroatoms selected from O, N and S and any aryl ring in R^7 is optionally substituted by R^a and/or R^b); C_{2-4}alkenyl; halogen; -(CH$_2$)$_y$COOR^8 (where y = 0-3 and R^8 represents H, C_{1-4}alkyl, or C_{2-4}alkenyl); -CONR^{9}R^{10} (where R^9 and R^{10} independently represent H, C_{1-4}alkyl, C_{2-4}alkenyl, -O-C_{1-4}alkyl, -O-C_{2-4}alkenyl or -C_{1-3}alkylenePh (wherein Ph is optionally substituted by R^a and R^b as hereinabove defined); -CON(R^{11})OR^{12} (where R^{11} and R^{12} independently represent H, C_{1-4}alkyl or C_{2-4}alkenyl);

a group of Formula II: -CONR^{13}-CR^{13a}R^{14}-COOR^{17}, (where R^{13} and R^{13a} are independently H or C_{1-4}alkyl, R^{17} is H or C_{1-6}alkyl, R^{14} is selected from the side chain of a lipophilic amino

acid, carbamoylC_{1-4}alkyl, N-(monoC_{1-4}alkyl)carbamoylC_{1-4}alkyl and N-(diC_{1-4}alkyl)carbamoylC_{1-4}alkyl, the group of Formula II having L or D configuration at the chiral alpha carbon in the corresponding free amino acid; a lactone of formula:



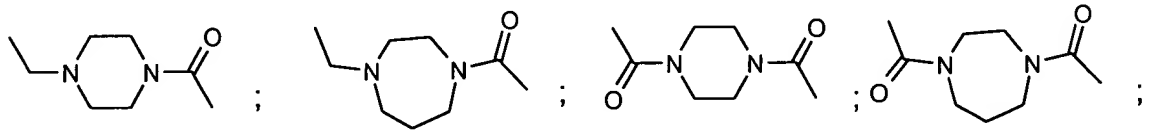
;

C_{1-4}alkyl monosubstituted on carbon with =N-OH;

a group of Formula -X-R^{15} (where X is selected from O, CO, CH_2, S, SO, SO_2 and R^{15} is selected from C_{1-6}alkyl, phenyl, naphthyl, a 5-10 membered monocyclic or bicyclic heteroaryl ring containing up to 5 heteroatoms selected from O, N and S and any aryl ring in R^{15} is optionally substituted by R^a and/or R^b;

p is 0-3 in which R^3 values can be the same or different;

G is a linking moiety selected from the following groups written from left to right in Formula I:



(wherein the piperazine and perhydro-1,4-diazepine rings are optionally substituted);

-CO-NR^{16}-; -CH_2-NR^{16}- ; -CH_2S-; -CH_2O-; -CH_2-CHR^{16}; -CH=CR^{16}-; -CH_2NR^{16}-T-; -CH_2NR^{16}-SO_2-; -CH_2-NR^{16}-CO-T^1-; -CO-NR^{16}-T-; -CH_2S-T-; -CH_2O-T- (where R^{16} is selected from H, C_{1-4}alkyl, C_{1-4}alkylene-Z, -CO-C_{1-4}alkylene-Z, -CO-C_{1-6}alkyl, -COZ, Z and Z is selected from -O-C_{1-4}alkyl, phenyl, naphthyl, a 5-10 membered monocyclic or bicyclic heteroaryl ring containing up to 5 heteroatoms selected from O, N and S and any aryl ring in R^{16} is optionally substituted by R^a and/or R^b as hereinabove defined;

where, T represents -$(CH_2)_m$- where m is 1-4 and T is optionally monosubstituted with any value of R^{16} other than H; and

where T^1 represents -$(CH_2)_{m^1}$- wherein m^1 is 0-4 and T^1 is optionally monosubstituted with any value of R^{16} other than H);

A is selected from phenyl; naphthyl; a 5-10 membered monocyclic or bicyclic heteroaryl ring containing up to 5 heteroatoms where the heteroatoms are independently selected from O, N & S;

or a -S-S- dimer thereof when R^2=H; or a N-oxide thereof;

or a pharmaceutically acceptable salt, prodrug or solvate thereof.

Please further amend the first paragraph on page 4, line 10 to page 6, line 11, as follows:

(Twice Amended) In another aspect of the invention there is provided an inhibitor of ras farnesylation of Formula I

wherein:

R^1 is selected from H; -C_{1-4}alkyl; -C_{1-3}alkylene-Ph optionally mono or di-substituted on Ph with substituents selected from C_{1-4}alkyl, halogen, OH, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, amino, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, C_{1-4}alkanoylamino, nitro, cyano, carboxy, carbamoyl, C_{1-4}alkoxycarbonyl, thiol, C_{1-4}alkylsulfanyl, C_{1-4}alkylsulfinyl, C_{1-4}alkylsulfonyl and sulfonamido; -CO-C_{1-4}alkyl; -CO-O-C_{1-4}alkyl; -CO-O-C_{2-4}alkenyl; -CO-O-$(CH_2)_n$Ph optionally substituted on Ph as defined for substitution on Ph in R^1 = -C_{1-3}alkylene-Ph above and n=0-4;

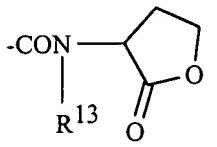
-C_{1-4}alkylene-$CONR^4R^5$ where R^4 & R^5 are independently selected from H and C_{1-4}alkyl; and -C_{1-4}alkylene-$COOR^6$ where R^6 is selected from H, C_{1-4}alkyl;

R^2 is selected from H; -C_{1-4}alkyl; -C_{1-3}alkylene-Ph optionally substituted on Ph as defined for substitution on Ph in R^1 = -C_{1-3}alkylene-Ph above; -COC_{1-4}alkyl; and -$COOC_{1-4}$alkyl;

R^3 is selected from H; OH; CN; CF_3; NO_2; -C_{1-4} alkyl; -C_{1-4}alkylene-R^7 where R^7 is selected from phenyl, naphthyl, a 5-10 membered monocyclic or bicyclic heteroaryl ring containing up to 5 heteroatoms selected from O, N and S and any aryl ring in R^7 is optionally substituted as defined for substitution on the Ph group in R^1 = -C_{1-3}alkylene-Ph above; R^7; C_{2-4}alkenyl; halogen; -$(CH_2)_yCOOR^8$ where y= 0-3 and R^8 represents H, C_{1-4}alkyl, or C_{2-4}alkenyl; -$CONR^9R^{10}$ where R^9 and R^{10} independently represent H, C_{1-4}alkyl, C_{2-4}alkenyl, -O-C_{1-4}alkyl, -O-C_{2-4}alkenyl, -C_{1-3}alkylenePh optionally substituted as defined for this group

for R^1 above; -CON(R^{11})OR^{12} where R^{11} and R^{12} independently represent H, C_{1-4}alkyl and C_{2-4}alkenyl;

a group of Formula II, -CONR^{13}-CHR^{14}-COOR^{17} , where R^{13} is H or C_{1-4}alkyl, R^{17} is H or C_{1-6}alkyl, R^{14} is selected from the side chain of a lipophilic amino acid, carbamoylC_{1-4}alkyl, N-(monoC_{1-4}alkyl)carbamoylC_{1-4}alkyl and N-(diC_{1-4}alkyl)carbamoylC_{1-4}alkyl, the group of Formula II having L or D configuration at the chiral alpha carbon in the corresponding free amino acid; a lactone of formula



;

C_{1-4}alkyl monosubstituted on carbon with =N-OH;

a group of Formula -X-R^{15} where X is selected from O, CO, CH_2, S, SO, SO_2 and R^{15} is selected from C_{1-6}alkyl, phenyl, naphthyl, a 5-10 membered monocyclic or bicyclic heteroaryl ring containing up to 5 heteroatoms selected from O, N and S and any aryl ring in R^{15} is optionally substituted as defined for the Ph group in R^1 = -C_{1-3}alkylene-Ph;

p is 0-3 in which R^3 values can be the same or different;

G is a linking moiety selected from the following groups written from left to right in Formula I:

-CO-NR^{16}- where R^{16} is selected from H, C_{1-4}alkyl, C_{1-4}alkylene-Z, -CO-C_{1-4}alkylene-Z, -CO-C_{1-6}alkyl, -COZ, Z and Z is selected from -O-C_{1-4}alkyl, phenyl, naphthyl, a 5-10 membered monocyclic or bicyclic heteroaryl ring containing up to 5 heteroatoms selected from O, N and S and any aryl ring in R^{16} is optionally substituted as defined for the Ph group in R^1 = -C_{1-3}alkylene-Ph; -CH_2-NR^{18}- where R^{18} represents any value defined for R^{16}; -CH_2S-; -CH_2O-; -CH_2-CHR^{19}- where R^{19} represents any value defined for R^{16}; -CH=CR^{20}- where R^{20} represents any value defined for R^{16}; -CH_2NR^{21}-T- where R^{21} represents any value defined for R^{16}, T represents -$(CH_2)_w$- where w is 1-4 and T is optionally monosubstituted with R^{22} where R^{22} represents any value for R^{16} other than H; -CH_2NR^{23}-SO_2- where R^{23} represents any value defined for R^{16}; -CH_2-NR^{24}-CO-T- where R^{24} represents any value defined for R^{16}, T represents -$(CH_2)_w$- where w is 0-4 and T is optionally monosubstituted

with R^{29} where R^{29} represents any value for R^{16} other than H; -CO-NR^{25}-T- where R^{25} represents any value defined for R^{16}, T represents -$(CH_2)_w$- where w is 1-4 and T is optionally monosubstituted with R^{26} where R^{26} represents any value for R^{16} other than H; -CH_2S-T- where T represents -$(CH_2)_w$- where w is 1-4 and T is optionally monosubstituted with R^{27} where R^{27} represents any value for R^{16} other than H; -CH_2O-T- where T represents -$(CH_2)_w$- where w is 1-4 and T is optionally monosubstituted with R^{28} where R^{28} represents any value for R^{16} other than H;

A is selected from phenyl; naphthyl; a 5-10 membered monocyclic or bicyclic heteroaryl ring containing up to 5 heteroatoms where the heteroatoms are independently selected from O, N & S;

or a -S-S- dimer thereof when R^2=H; or a N-oxide thereof;

or an enantiomer, diastereoisomer, pharmaceutically acceptable salt, prodrug or solvate thereof.

Please further amend the first paragraph on page 10, line 4 to page 10, line 15, as follows:

(Twice Amended) Suitable values for G= CH_2NR^{16} T include CH_2.N(CO.CH_2.$CHMe_2$).CH_2.CH_2; CH_2.N(CH_2 CH_2 CH_2OMe).CH_2.CH_2; CH_2.N(CH_2.*p*Ph.OMe).CH_2.CH_2; CH_2.N(CO.CH_2.$CHMe_2$).CH_2; CH_2N(CO.CH_2.CH_2.CH_2.Me).CH_2; CH_2N(CO.CH_2.CHMe.CH_2Me).CH_2; CH_2N(CO.CH_2.CH_2.OMe)CH_2; CH_2N(CO.CH_2.pyridin-3-yl).CH_2; CH_2N(4-methoxybenzyl)CH_2; CH_2N(CO.CH_2.$CHMe_2$)CH_2.CH_2.CH(Ph); CH_2N(CO.CH_3)CH_2.CH_2.CH(Ph); CH_2N(CO.CH_2.$CHMe_2$)CH_2; CH_2N(CO.CH_3)CH_2; CH_2N(CO.CH_2.$CHMe_2$)CH_2.CH(Ph); CH_2N(CO.CH_2.CMe_3)CH_2.CH(Ph); CH_2N(CO.CH_2.pyridin-3-yl)CH_2.CH(Ph); CH_2N(CO.1-hydroxy-6-methoxy-pyridin-3-yl)CH_2.CH(Ph); CH_2N(CO.CH_2 pyrid-3-yl)CH_2CH(Ph); CH_2N(CO.$CH_2$$CHMe_2$)$CH_2$.$CH_2$; CH_2N(CO.$CH_2$$CMe_3$)$CH_2$.$CH_2$; CH_2N(CO thiazol-2-yl)CH_2CH_2; CH_2N(CO 1-oxido-6-hydroxypyridin-3-yl)CH_2CH_2; CH_2N(CO.CH_2pyridin-3-yl)CH_2.CH_2 and CH_2N(CO.4-methoxybenzyl)CH_2.CH_2.

Please further amend the third paragraph on page 10, line 20 to page 10, line 22, as follows:

(Twice Amended) Suitable values for G = $-CH_2NR^{16}-$ include CH_2NH; CH_2NMe; $CH_2N(CO.CH_2.CHMe_2)$ and $CH_2N(CO.CH_2.CH_2.OMe)$. A preferred value for $-CH_2NR^{16}-$ is $-CH_2NH-$.

Please further amend the fourth paragraph on page 10, line 23 to page 10, line 26 as follows:

(Twice Amended) When G is $-CH_2NR^{16}-T-$ a suitable value for m is 1. When G is $-CH_2-NR^{16}-CO-T^1-$ a suitable value for m^1 is 1. When G is $-CH_2-NR^{16}-T-$ a suitable value for m is 1. When G is $-CH_2-S-T-$ a suitable value for m is 1. When G is $-CH_2-O-T-$ a suitable value for m is 1.

G is especially $-CONH-$, $-CH_2.NH-$, $-CH_2NHSO_2-$, $-CH_2NHCO-$.

Please further amend the first paragraph on page 32, line 4 to page 32, line 23, as follows:

(Twice Amended) Compounds of Formula I in which G represents $-CO-NR^{16}-$ may be prepared by forming an amide bond between compounds 1 and 2 as outlined in Scheme 1. Compounds of Formula I in which G represents $-CO-NR^{16}-T-$ may be prepared by an analogous procedure. Suitable coupling conditions include the following.

i) Use of EEDQ at ambient temperature in an organic solvent (e.g. dichloromethane, methanol).

ii) Use of oxalyl chloride in an organic solvent (e.g. CH_2Cl_2), DMF in a catalytic amount, in the presence of an organic base (e.g. NMM, triethylamine, DMAP) at 0°C to ambient temperature for 0.5-16h.

iii) Use of EDC/ HOBT in an organic solvent (e.g. DMF, CH_2Cl_2).

iv) Use of DCCI/ HOBT in an organic solvent (e.g. DMF, CH_2Cl_2) in the presence of an organic base (e.g. triethylamine).

v) Use of mixed anhydride reactions under standard conditions, for example isopropylchloroformate in an organic solvent (e.g. DMF, DMA, dichloromethane) in the presence of an organic base (e.g. NMM, DMAP, triethylamine).

06 vi) Via an active ester under standard conditions e.g. pentafluorophenyl ester in an organic solvent (e.g. dichloromethane) in the presence of an organic base (e.g. triethylamine).

vii) Via an acid chloride under standard conditions e.g. using thionyl chloride and heat for about 150min followed by an organic base (e.g. triethylamine) in the presence of an organic solvent (e.g. acetonitrile).

Please further amend the second paragraph on page 32, line 24 to page 33, line 3, as follows:

(Twice Amended) Compounds of Formula I in which G represents $-CH_2NR^{16}-$, $-CH_2O-$ or $-CH_2S-$ may be prepared as outlined in Scheme 2. LG represents a leaving group (e.g. mesyloxy, tosyloxy, halogen) and X represents S, O or NR^{16}. Suitable coupling conditions include the following.

07 i) Use of an inorganic base (e.g. $NaHCO_3$, NaH, K_2CO_3, butyllithium) in an organic solvent (e.g. THF, DMF, DMSO) and a temperature of about 65° to 150°C

ii) Use of an organic base (e.g. triethylamine, DMAP) in an organic solvent (e.g. THF, dichloromethane, DMA, DMF) at a temperature range of room temperature -150°C

iii) Use of an inorganic base (e.g. KOH, NaOH, K_2CO_3) in an aqueous (e.g. water) and organic solvents (e.g. dichloromethane) in a 2 phase system, optionally in the presence of a phase transfer catalyst (e.g. tetrabutylammoniumbromide).

Please further amend the second paragraph on page 33, line 13 to page 33, line 18, as follows:

(Twice Amended) Compounds of Formula I in which G represents $-CH_2-NR^{16}-$ may

08 be prepared as outlined in Scheme 4 by coupling aldehyde (2) with compound 4. Suitable coupling conditions include the following.